60 days of head-down bedrest differentially alters venous function in lower but not upper body between healthy men and women

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The incidence of orthostatic intolerance after space flight is disproportionally higher in female compared to male crewmembers (83% vs. 20%). Experimental and human data suggest that the loss of orthostatic tolerance is due, at least in part, to microgravity-induced changes in venous compliance and that these changes are specific to the lower body. It is unknown however, whether the changes in venous compliance are different between males and females after space flight, and whether this is related to the disparity in orthostatic intolerance between the sexes. Using 6° head-down bed rest (BR) as a model of space flight, we tested the following hypotheses; 1) females, compared to males, would experience a greater increase in venous compliance in dorsal foot veins as an effect of BR and 2) no differences in venous compliance would be found in dorsal hand veins between sexes and across BR days. Using 2-D ultrasound, dorsal hand (DHV) and foot vein (DFV) responses (diameter; expressed as mm<sup>2</sup>) to 40 mmHg of congestion pressure (compliance) and to intravenous infusion of phenylephrine (PE; 3160ng/min) were determined in 10 females and 16 males before and after 60 days of BR. The relation between changes in vein diameter (in response to pressure and PE), sex, limb, and BR days were determined using a mixedeffect linear regression. It was found that after 60 days of BR, DFV dilator response to pressure was significantly greater in females and significantly less in males compared to pre-BR. As expected, there were no differences in DHV dilator response between sexes nor was there a significant difference between pre and post measures within groups. Notably, the venoconstrictor response to infusions of PE in the DHV and DFV where similar between sexes and across BR days. In conclusion, this study demonstrates that after 60 days of BR, dorsal foot veins are more compliant in women and less compliant in men. Moreover, the changes in lower body vein compliance in females do not appear to be due to changes in vasoconstrictor tone as their response to PE was preserved and similar to that in males. Taken together these data suggest that the higher incidence of orthostatic intolerance in females after space flight is due to increased venous compliance in the lower body which could translate to lower venous filling pressures and a reduced stroke volume.